Massachusetts Department of Public Health
Division of Epidemiology and Immunization

Recommendations for Use of Rotavirus Vaccine
-- Clinical Advisory --
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On February 3, 2006, the Food and Drug Administration licensed a rotavirus vaccine (RotaTeq®, manufactured by Merck) for use in infants 6 to 32 weeks of age. This vaccine is a live, oral, human-bovine reassortant vaccine. Four reassortant viruses express one of the major surface proteins (G1, G2, G3, G4) from the most common human rotavirus serotypes, and a fifth contains an attachment protein (P1A[8]) from the human rotavirus parent strain and the outer capsid protein (G6) from the bovine rotavirus parent strain.

Rotavirus typically causes gastroenteritis with fever, vomiting, diarrhea and dehydration. It affects almost all children by the age of 5 years, with most cases occurring between 6-24 months of age. Annually in the U.S., rotavirus gastroenteritis leads to about 60,000 hospitalizations, 600,000 emergency room and clinic visits, and 20-60 deaths.

In prelicensure studies, RotaTeq® had an overall vaccine efficacy of 74% and was 98% effective in preventing severe diarrhea. This vaccine also resulted in an 86% reduction in physician visits and 96% reduction in hospitalizations due to rotavirus infection.

In February 2006, the Advisory Committee on Immunization Practices (ACIP) voted to recommend routine immunization of all U.S. infants with rotavirus vaccine to prevent rotavirus gastroenteritis, and then published their final recommendations in the *Morbidity and Mortality Weekly Report* on August 11, 2006 (http://www.cdc.gov/mmwr/PDF/rr/rr5512.pdf).

Recommendations for use of Rotavirus Vaccine

1. Routine Immunization.
All infants should receive 3 doses of rotavirus vaccine (RotaTeq®) administered orally at 2, 4, and 6 months of age (with a minimum interval of 4 weeks). The first dose should be administered between 6-12 weeks of age. Subsequent doses should be administered at 4 to 10 week intervals. All 3 doses of vaccine should be administered by 32 weeks of age.

Vaccination should **not** be initiated for infants ≥ 13 weeks of age because of insufficient data about the safety of the 1st dose of rotavirus vaccine in older infants. Rotavirus vaccine should **not** be administered after 32 weeks of age because of the lack of both safety and efficacy data in older infants. (See below in the section on **Vaccine Safety** for additional information.)

Infants who are being breast fed can receive rotavirus vaccine. Like other vaccines, rotavirus vaccine can be administered to infants with transient mild illnesses (with or without low-grade fever), including mild acute gastroenteritis. The exception is acute, moderate to severe gastroenteritis (See below in the section on **Precautions** for additional information.)

- **Administration.** RotaTeq® is a pale yellow liquid that may have a pink tint. Each 2.0 mL dose is supplied in a squeezable plastic dosing tube with a twist-off cap, allowing for direct oral administration. Vaccine should be administered as soon as possible after being removed from the refrigerator.

- **Regurgitation of vaccine.** Re-administration of a dose of rotavirus vaccine to an infant who regurgitates, spits out, or vomits during or after administration of vaccine is **not** recommended. Data are limited regarding the safety of administering a dose of rotavirus vaccine higher than the recommended dose (as well as the efficacy of a partial dose). The infant should receive the remaining recommended doses of rotavirus vaccine at appropriate intervals.

- **Simultaneous administration.** Rotavirus vaccine can be administered together with other childhood vaccines indicated at the same visits, including *Haemophilus influenzae* type b conjugate (Hib) vaccine, inactivated poliovirus vaccine (IPV), hepatitis B (HepB) vaccine, pneumococcal conjugate vaccine (PCV), and the diphtheria, tetanus, and acellular pertussis (DTaP) vaccines.

The schedule for rotavirus vaccine is summarized in the table below.

Recommended Rotavirus Vaccine Schedule

Dose	Age (min/max)	Interval to Next Dose (min/max)
1	2 months (6 weeks/12 weeks)[1,2]	2 months (4 weeks/10 weeks)
2	4 months (10 weeks/22 weeks)	2 months (4 weeks/10 weeks)
3	6 months (14 weeks/32 weeks)[3]	NA

[1] The 1st dose **must** be given by 12 week of age.
[2] If the 1st dose is inadvertently administered at ≥ 13 weeks of age, the rest of the series can be completed per schedule. But, all doses **must** be received by 32 weeks of age.
[3] The 3rd dose **must** be given by 32 weeks of age, regardless of when the series began.

- **Shedding of vaccine virus in the stool.** Shedding of vaccine virus in the stool occurred in 8.9% of vaccine recipients tested after the 1st dose and in <1% after the 2nd and 3rd doses. Shedding was observed 1-15 days following a dose. Transmission of the vaccine virus to non-vaccinated contacts has not been studied.

2. Special Situations.

- **Premature infants (i.e., those born at <37 weeks' gestation).** Premature infants can be immunized if they are: a) at least 6 weeks of age; b) clinically stable; and c) being or have been discharged from the hospital nursery.

  Premature infants are at increased risk for hospitalization for gastroenteritis. Although relatively small numbers of preterm infants have been evaluated, safety and efficacy appear similar to term infants. Until further data are available, the ACIP considers that benefits of rotavirus vaccine for premature infants outweigh any theoretical risks.

- **Exposure of immunocompromised persons to vaccinated infants.** Infants living in households with persons who have or are suspected of having impaired immune status can be vaccinated. There is a small risk of transmitting vaccine virus to a household member, but vaccinating the infant protects that household member from exposure to wild rotavirus. Expert opinion supports the view that the benefits of vaccine outweigh the small risk of transmission.

  To minimize potential virus transmission, all household members should employ measures such as good hand washing after contact with feces of the vaccinated infant (e.g., after changing a diaper).

- **Exposure of pregnant women to vaccinated infants.** Infants living in households with pregnant women can be vaccinated.

  Most women of child-bearing age have preexisting immunity. The vaccine strains are attenuated and vaccinating young children even further reduces the potential exposure of pregnant women to the wild virus. In addition, no evidence exist that rotavirus infection or disease in pregnant women poses any risk to the fetus.

- **Hospitalization after vaccination.** If a child who has recently received rotavirus vaccine is hospitalized for any reason, no precautions other than routine standard precautions need be taken to prevent the spread of vaccine virus in the hospital setting.

3. Contraindications.

There are 2 contraindications to rotavirus vaccine:

- **History of an anaphylactic reaction to any component of the vaccine**. (While there are trace amounts of fetal bovine serum in rotavirus vaccine, there are no preservatives, thimerosal or latex.)
- **History of anaphylactic reaction to a previous dose of rotavirus vaccine**.

4. Precautions.

The following are precautions to rotavirus vaccine:

- **Altered immunocompetence**. Practitioners need to consider the potential risks and benefits of administering rotavirus vaccine to infants with known or suspected altered immunocompetence. Rotavirus gastroenteritis can sometimes be prolonged and severe in those who are immunocompromised. However, no data are yet available on the safety and efficacy of administration of rotavirus vaccine to infants who are potentially immunocompromised, including:
  - infants with blood dyscrasias, leukemia, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic system;
  - infants on immunosuppressive therapy (including high-dose systemic corticosteroids);
  - infants with primary and acquired immunodeficiency states, including infection with human immunodeficiency viruses; cellular immune deficiencies; hypogammaglobulinemic and dysgammaglobulinemic states; and infants with indeterminant HIV status who are born to mothers with HIV infection; and
  - infants who have received a blood transfusion or blood products, including immunoglobulins, within 42 days.
- **Moderate to severe illness (with or without fever), including acute, moderate to severe gastroenteritis**. As with other vaccines, these infants can be vaccinated with rotavirus vaccine as soon as they have recovered.

  Use of rotavirus vaccine in patients with moderate to severe gastroenteritis is not well studied. Immunogenicity and efficacy can be theoretically compromised. (For example, infants who receive oral polio [OPV] vaccine during an episode of acute gastroenteritis in some instances have had diminished antibody responses to OPV.) As stated above, these infants can be vaccinated as soon as they have recovered from episodes of moderate to severe gastroenteritis.

  Please note, infants with mild acute gastroenteritis can be vaccinated, particularly if the delay in vaccination might be substantial and make the child ineligible to receive vaccine (e.g., age $\geq$ 13 weeks before vaccination is initiated).
- **Preexisting chronic gastrointestinal (GI) disease**. The safety and efficacy of rotavirus vaccine has not been well studied in infants with preexisting GI disease (e.g., congenital malabsorption syndromes, Hirschsprung's disease, short-gut syndrome, or persistent vomiting of unknown cause). According to the ACIP, in infants with chronic GI disease without immunosuppression, benefits from rotavirus vaccination outweigh the theoretical risks from the vaccine.
- **Previous history of intussusception**. Infants with a history of intussusception might be at higher risk for a repeat episode. Therefore, until postlicensure data on safety of rotavirus vaccine are available, the risks for and the benefits of vaccination should be considered when vaccinating infants with a previous episode of intussusception. (See below in the section on **Vaccine Safety** for additional information.)

5. Vaccine Safety.

Following administration of a previously licensed, rhesus-based rotavirus vaccine, RRV-TV (RotaShield® by Wyeth), an increased risk for intussusception was observed. The greatest risk occurred 3-14 days after the 1st dose and risk increased with age, with infants >90 days old accounting for 80% of the cases.

Available prelicensure data from a RotaTeq® trial of 70,000 infants found no evidence of an association between intussusception and the current vaccine (within 1 year of the 1st dose, there were 13 cases in the vaccine group and 15 in the placebo group).

However, additional postlicensure surveillance data are required to confirm that the vaccine is not associated with intussusception at a lower rate than would have been detected in prelicensure trials. In addition, data suggest that infants with a history of intussusception might be at higher risk for a repeat episode than other infants. Therefore, until postlicensure data on safety of rotavirus vaccine are available, the risks for and the benefits of vaccination should be considered when vaccinating infants with a previous episode of intussusception.

In prelicensure studies, RotaTeq® was very well tolerated and had an acceptable safety profile. Most adverse events were similar in both vaccine and placebo groups, except for diarrhea (18% vs 15%) and vomiting (12% vs 10%), which both had slightly higher rates in the RotaTeq®group.

Intensive postlicensure vaccine safety surveillance will be needed and is currently underway, including studies being conducted by Merck and those being coordinated by Centers for Disease Control and Prevention (CDC) among those enrolled in the health plans participating in the Vaccine Safety Datalink (VSD) project. Recently developed rapid analysis methods allow the VSD to conduct near "real time" monitoring for vaccine adverse events.

Vaccine Information Statements

An interim vaccine information statement (VIS) for rotavirus was issued on April 12, 2006 and is available at: www.immunize.org/vis. In the future, a *final* VIS will be re-published with a new date and a copy will be available at the above website.

Reporting of Adverse Events after Vaccination

Enhanced postlicensure surveillance for adverse events following RotaTeq® is underway.
It is important for all clinically significant adverse events to be reported to VAERS, even if a causal relationship to vaccination is uncertain. VAERS reporting forms and information are available electronically at: http://vaers.hhs.gov/ or by calling (800) 822-7967. Providers are encouraged to report electronically at: https://secure.vaers.org/VaersDataEntryintro.htm.

Availability and Ordering of Rotavirus Vaccine Supplied by MDPH

In late August 2006, MDPH began supplying limited amounts of rotavirus vaccine for infant immunization. At this time, the only funds available for the state purchase of rotavirus vaccine are from the federal entitlement Vaccines for Children (VFC) Program. The VFC program provides vaccines free-of-charge for children under 19 years of age who are: a) enrolled in Medicaid; b) without health insurance; c) American Indian or Alaska Native; or c) seen at federally qualified community health centers. MDPH will secure as many doses as funding will allow from the federal CDC contract for the VFC-eligible cohort.

Health plans and insurance carriers have been informed of the groups for whom MDPH will be supplying rotavirus vaccine and the need for providers to purchase rotavirus vaccine for their non-VFC-eligible children. The Current Procedural Terminology (CPT®) code for RotaTeq® is 90680. RotaTeq® can be ordered from Merck (1-800-672-6372) or at their website (https://www.merckvaccines.com/).
For inventory management purposes, providers will need to be able to distinguish between state-supplied vaccine and private purchase vaccine

Rotavirus vaccine should be stored at refrigerator temperatures (36^0F-46^0F [2^0C-8^0C]). If you have questions about the recommendations for use and the availability of state-supplied rotavirus vaccine, please call the MDPH Immunization Program at 617-983-6800 or 888-658-2850.